UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Andres Garzon Moreno, Entomologist

From: Frank Antwi, Ph.D. Entomologist

Secondary Review: Jennifer Saunders, PhD, Senior Biologist

Date: 8/10/2020

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER DOES NOT CONTAIN CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 457446
Decision no.: 561940
Submission no: 1049714
Action code: R340
Product Name: ZYROX Fly Granular Bait
EPA Reg. No or File Symbol: 100-1541
Formulation Type: Bait
Ingredients statement from the label with PC codes included:
Active ingredient: cyantraniliprole (0.5%); PC code: 090098

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate):
0.2 to 0.4 lbs (pounds) per 1000 square feet.

Use Patterns:
Granular insect bait for use in and around residential, commercial, institutional, and agricultural structures to control fly and cockroach pests.

I. Action Requested:
The registrant is requesting to add new pest species to their product Zyrox Fly Granular Bait label (EPA Reg. No. 100-1541). The registrant has submitted efficacy data and has proposed to add the claim of kills cockroaches to the label.

II. Background:
The registrant has submitted efficacy data that they claim demonstrates that Zyrox Fly Granular Bait is highly attractive or palatable, and effective in killing cockroaches. Based on these studies, the registrant

has proposed to add the claim of kills cockroaches to the label.

III. MRID Summary:
MRID 51052801. Cartwright, B. (2020). Zyrox (A20780A) efficacy data to support use of cyantraniliprole Bait against cockroaches. Report Number TK0541185. Unpublished trial report prepared for Syngenta Crop Protection, LLC, Greensboro NC. 135p. [Appendices 1, 2, 3, and 4]

Appendix 1.
Bibbs, C. S. (2019). Efficacy of cyantraniliprole formulated as a bait against German cockroaches. Trial Report number WM5913.

(1) **non-GLP**

(2) **Methods:**

Mixed sex, adult, non-gravid German cockroaches (*Blatella germanica*) were randomly collected from in-house colonies and separated into cohorts of 10 individuals. The evaluations were conducted in choice arenas 6 inches by 6 inches (0.25 feet square). Folded, cardboard harborages were placed in one corner of the test arena. Cockroach food was placed in an adjacent corner. Treatment was placed in a corner opposite, and equidistant from the harborage. Water was placed in the corner opposite the harborage. Ten organisms were introduced into the arena already containing food and water. The test substance 22.7 mg (3.2 oz/1,000 feet square) was placed in an assigned corner of the test arena after 24 hours. Water, test substance, and non-insecticidal food were replaced as consumed. The number of alive, moribund, and dead organisms were recorded daily for 14 days (days 1 to 14) post-treatment. Hereafter, we present results for 1, 3, 7, 10, and 14 days post treatment exposure. A negative control arena (with no treatment) was assigned for every product test arena. Both treatment and control each had 7 replicated arenas, each containing 10 mixed sex, adult, non-gravid German cockroaches (*Blatella germanica*) cockroaches. The initial treatment of 22.7 mg of granule was not completely consumed during study. Consequently, no replacement treatments were made after the first treatment day.

Percent mortality was calculated using the following formula: % Mortality = ((1-(C/D)) x 100; whereby C = number of live arthropods; and D = total number of arthropods. Abbott's formula (Abbott 1925) was used to account for control mortality as ((A- B) /A)) x 100; whereby A = % alive in control; and B = % alive in treatment.

(3) **Results:**

During treatment evaluation, 1.4% control mortality was observed. Treatment with Zyrox resulted in over 95.7 to 100% mortality against German cockroaches (*Blattella germanica*) at 10 to 14 days post-treatment (Table 1).

Table 1. Percent mortality of German cockroach adults with Zyrox (cyantraniliprole) Fly Granular Bait.

	% Mortality				
Treatment	**Day 1**	**Day 3**	**Day 7**	**Day 10**	**Day 14**
Control	0.0	0.0	1.4	1.4	1.4
A20780A (Zyrox Fly Granular Bait)	7.1	30.0	78.6	95.7	100.0

(4) **Conclusion: Partially Acceptable.** Cyantraniliprole formulated at 0.5% as a granular bait was effective against German cockroaches (*Blattella germanica*). Zyrox at an application rate of 3.2 oz/ l000 feet square killed German cockroaches (*Blattella germanica*) with 95.7 to 100% mortality at 10 to 14 days post-treatment application. The data submitted supports indoor kills of German cockroach adults for Zyrox at 3.2 oz/ l000 feet square at 10 - 14 days post-treatment application.

[Appendix 2]
Bibbs, C. S. (2019). Efficacy of cyantraniliprole formulated as a bait against Oriental cockroaches. Trial Report number: WM5915.

(1) **non-GLP**

(2) **Methods:**

Mixed sex, adult, non-gravid Oriental cockroaches (*Blatta orientalis*) were randomly collected from in-house colonies and separated into cohorts of 10 individuals. A choice test studies were conducted in arenas with dimensions 6 inches by 6 inches (0.25 feet square). Folded, cardboard harborages were placed in one corner of the test arena. Cockroach food was placed in an adjacent corner. Treatment was placed in a corner opposite, and equidistant from the harborage. Water was placed in the corner opposite the harborage. Ten organisms were introduced into the arena already containing food and water. The test substance 22.7 mg (3.2oz/1,000 feet square) was placed in an assigned corner of the test arena after 24 hours. Water, test substance, and non-insecticidal food were replaced as consumed. The number of alive, moribund, and dead organisms were recorded daily for 14 days (days 1 to 14) post-treatment. A negative control arena (with no treatment) was assigned for every product test arena. Both treatment and control each had 7 replicated arenas, each containing 10 mixed sex, adult, non-gravid Oriental cockroaches (*Blatta orientalis*).
Percent mortality was calculated using the following formula: % Mortality = ((1-(C/D)) x 100; whereby C = number of live arthropods; and D = total number of arthropods. Abbott's method (Abbott 1925) as ((A- B) / A) x 100 was used to account for control mortality; whereby A = % alive in control; and B = % alive in treatment.

(3) **Results:**
Due to habituation and mortalities in replicates 3, 4, and 7, three additional replicates (8, 9, and 10) were conducted. In view of this the reviewer went into the raw data submitted and used replicates (1, 2, 5, 6, 8, 9, and 10) to calculate percentage mortalities and accounted for control mortalities with the Abbott

method. Hereafter, results are presented for days 1, 3, 5, and 7 (Table 2).

During treatment evaluation, 1.43% control mortality was observed at days 3 to 7 (Table 2). Treatments resulted in 95.65% mortality against Oriental cockroaches (*Blatta orientalis*) at day 7 (Table 2). The treatment of 22.7 mg of granule was replaced twice after the initial treatment for all included replicates. It was not necessary to replace treatments after day 3 of study.

Table 2. Percent mortality of Oriental cockroach adults with Zyrox (cyantraniliprole) Fly Granular Bait.

	% Mortality			
Treatment	**Day 1**	**Day 3**	**Day 5**	**Day 7**
Control	0	1.43	1.43	1.43
A20780A (Zyrox Fly Granular Bait)	5.71	52.17	85.06	95.65

(4) **Conclusion: Partially Acceptable.** Cyantraniliprole formulated at 0.5% as a granule was effective against oriental cockroaches (*Blatta orientalis*) with two reapplications at a rate of 3.2 oz/1,000 ft^2. Application of Zyrox (0.5%; at 3.2 oz/1000 ft^2) resulted in 95.7% mortality of Oriental cockroaches (*Blatta orientalis*) at 7 days post-treatment. The data submitted supports indoor kills of Oriental cockroach adults for Zyrox at 3.2oz/ l000 feet square at 7 days post-treatment application. However, the bait should not have been replenished; see the OCSPP 810.3500 Premises Treatment guideline. The study is partially acceptable if the label language "Reapply bait every 7 days until insect pest population is at acceptable levels" is changed to "Reapply as needed".

[Appendix 3]
Trial Report #WM5914. Bibbs, C. S. (2019). Efficacy of cyantraniliprole formulated as a bait against American cockroaches.

(1) **non-GLP**

(2) **Methods:**

Mixed sex, adult, non-gravid American cockroaches (*Periplaneta americana*) were randomly collected from (Benzon Research Inc. colonies) and were separated into cohorts of 10 individuals. Arenas (14 inches x 8 inches x 4.9 inches; 0.78 feet square) were used for evaluations in a choice test assay. Folded, cardboard harborages were placed in one corner of the test arena with cockroach food in an adjacent corner. Treatment was placed in a corner opposite, and at equal distant from the harborage, and with water placed in the corner opposite the harborage. Ten organisms were introduced into the arena. The test substance (cyantraniliprole 0.5 %; 70.6 mg (3.2 oz/1,000 feet square)) was placed in an assigned corner of the test arena after 24 hours. Water, test substance, and non-insecticidal food were replaced as consumed. The number of alive, moribund, and dead organisms were recorded daily for 28 days post-treatment. The treatment was removed after collecting the day-14 data. Test organisms were moribund, and below the 90% mortality, so food and water, were continuously supplied for a total of 28 days until

morbidity was resolved as either recovery or mortality. A negative control arena (with no treatment) was assigned for every product test arena, carried out and data recorded daily for 28 days. There were 7 replications for both treatment and control. Each replicated arena contained 10 mixed sex, adult, non-gravid American cockroaches (*Periplaneta americana*). Hereafter, results are presented for days 1, 3, 7, 14, 21, and 28 days post-treatment application.

Percent mortality was calculated using the formula: % Mortality = ((1-(C/D)) x 100; whereby C = number of live arthropods; and D = total number of arthropods. Abbott's formula as: ((A- B) / A)) x 100; whereby A = % alive in control; and B = % alive in treatment was used to account for control mortality.

Methods Justification:
The Author(s) justified moribund and mortality delay per the statement and reference (Appel and Smith 1996), as "American cockroaches (*Periplaneta americana*) may exist in the moribund condition for several days before death occurs. Smith and Appel (1996) describe as much as a 66-day delay in mortality among American cockroaches (*Periplaneta americana*), with variable rates across a wide array of commercialized baits. To avoid inaccurate assessment of whether the cyantraniliprole bait is toxic to American cockroaches (*Periplaneta americana*), observations were carried out until obviously moribund cockroaches either recovered or died to an extent to decide if 90% mean mortality was achievable". The reviewer is of the view that in addition to the reference, the mode of action of cyantraniliprole through unregulated activation of insect ryanodine receptor channels, leading to internal calcium store depletion and impaired regulation of muscle contraction, causing paralysis and eventual death of the insect would have been a more appropriate justification for delayed mortality.

(3) **Results:**
Control mortalities were 1.4% at day 28 (Table 3). Per the raw data submitted moribund American cockroaches ranged from 0 to 37.14% at days 1 to 14 post-treatment application (Table 3). Percentage moribund cockroaches then decreased from 37.14% to 2.86% at 14 to 28 days post-treatment application (Table 3). Treatments resulted in over 97.1% mortality against American cockroaches (*Periplaneta americana*) at day 28 (Table 3). The treatment of 70.6 mg of granule was replaced 9 times after the initial treatment for all included replicates (days 2-8, 10, and 12).

Table 3. Percentage mortality of American cockroach adults with Zyrox (cyantraniliprole) fly granular bait.

		% Mortality[a]				
Treatment	**Day 1**	**Day 3**	**Day 7**	**Day 14**	**Day 21**	**Day 28**
Control	0	0.0	0.0	0.0	0.0	1.4
A20780A (Zyrox Fly Granular Bait)	0 (0)	5.71 (0)	12.86 (5.71)	42.83 (37.14)	74.29 (21.43)	97.10 (2.86)

[a] % Mortality: Numbers in brackets represent % moribund American cockroaches.

(4) **Conclusion: Partially Acceptable.** Cyantraniliprole (0.5%) as a granule was effective against American cockroaches (*Periplaneta americana*) with 9 reapplications at a rate of 3.2oz/1,000ft^2.

Cyantraniliprole treatments resulted in 97.1% mortality against adult American cockroaches (*Periplaneta americana*) at 28 days post-treatment application. Cyantraniliprole (0.5%; 3.2oz/1,000ft^2) was effective for killing American cockroach (*Periplaneta americana*) adults at 28 days after application. The data submitted supports indoor kills of American cockroach adults for Zyrox at 3.2oz/ l000 feet square at 28 days post-treatment application. However, the bait should not have been replaced 9 times after the initial treatment; see the OCSPP 810.3500 Premises Treatment guideline. The studies is partially acceptable if the label language "Reapply bait every 7 days until insect pest population is at acceptable levels" is changed to "Reapply as needed".

Appendix 4
Romero, A. (2017). Laboratory comparison of German cockroach feeding preferences for several cockroach baits. Trial Report number: PPMU17230.

(1) **non-GLP**

(2) **Methods:**

Insects from the Bakersfield strain of German cockroaches maintained since 2014 in the laboratory was used. This colony is reported to have intermediate levels of physiological resistance to indoxacarb. Fourteen replicates (7 females, 7 males) were completed. The treatments used are as detailed below:

1. A20379A (Advion Cockroach Gel Bait)
2. A20379E (Advion Evolution Cockroach Gel Bait)
3. A15276C (Optigard Cockroach Gel Bait)
4. Maxforce FC Magnum - fipronil
5. Vendetta Plus- Abamecttin B1, Pyriproxyfen
6. Zyrox Fly granular bait (cyantraniliprole)
7. Cockroach regular food (rabbit, dog, cat feed and sweetened corn puff cereals (1: 1: 1: 1).

A plastic cake container (Mainstays, Bentonville, AR) lined with white filter paper (29.2 cm diameter) was used as the test arena. Seven white filter papers of diameter 3 cm were placed concentrically at 3.8 cm away from the container wall. The filter papers were separated from each other by 4.9 cm, and the distance between edges of filter papers and the center of the arena was 7 cm. Each of the seven test materials (0.5 g) was placed on each filter paper and their position was rotated clockwise between replicates. Individual cockroaches were used per replicate and had an acclimation time of 5 min before release.

A high-resolution monochrome camera (Ikegami Electronics Inc., Maywood, NJ) with a variable focal TV lens (4.5-12.5MM F1.2; Computar, Cary, NC) and an infrared pass filter (Heliopan, North White Plains, NY) were used to record cockroach activity in the arena. The camera was suspended 82 cm above the arena using a stand. Light for the recordings was provided by two infrared illuminators (AXTON, North Salt Lake, UT) positioned above the arena at 80 cm. EthoVision XT version 11.5 software (Noldus Information Technology Inc. Leesburg, VA) was used to capture video images tracking the cockroaches during 20-min bioassays. Seven virtual filter papers were delimitated with the software and the behavioral parameters: latency (time to make first contact with bait), number of visits, and time spent in each bait zone were estimated for each bait. Laboratory conditions were (temperature 26 °C, and relative humidity 40%).

(3) **Results:**
German cockroaches took significantly less time to reach A20379A, A15276C, and Zyrox than cockroach food (food regularly used to maintain the colony) ($P < 0.05$).

Latency (time to make first contact with bait)
When latency was compared across baits, pairwise comparison analysis showed that cockroaches took less time to visit Zyrox than A20379A, MaxForce and Vendetta ($P < 0.05$) (Table 1). No significant difference was observed in other pairwise analysis (Table 1).

Table 1. Matrix with statistical comparison (not different or DIFFERENT) of latency of cockroaches to baits.

	A20379A	A20379E	A15276C	Zyrox	MaxForce	Vendetta
A20379A						
A20379E	Not different					
A15276C	Not different	Not different				
Zyrox	Not different	DIFFERENT	Not different			
MaxForce	Not different	Not different	Not different	DIFFERENT		
Vendetta	Not different	Not different	Not different	DIFFERENT	Not different	

Number of visits to test material
Total number of visits made by cockroaches to each test material zone indicates how attractive the materials were to the cockroaches. **Paired-comparison analysis showed that cockroaches visited A20379A, A20379E, A15276C, or Zyrox significantly more than roach food ($P < 0.05$).** Comparison among baits showed that visits by cockroaches did not differ significantly (Table 2).

Table 2. Matrix with comparison of visitation rates of cockroaches to baits

	A20379A	A20379E	A15276C	Zyrox	MaxForce	Vendetta
A20379A						
A20379E	Not different					
A15276C	Not different	Not different				
Zyrox	Not different	Not different	Not different			
MaxForce	Not different	Not different	Not different	Not different		
Vendetta	Not different	Not different	Not different	Not different	Not different	

Time spent on test material
The more time the insect remained arrested in the zone, the more palatable the material was. A paired comparison analysis showed that cockroaches spent significantly more time in zones with A20379A, A20379E, and Zyrox than in zones with cockroach food ($P < 0.05$). Pairwise comparison between baits showed that the cockroaches spent significantly more time in zones with A20379A than MaxForce or Vendetta ($P < 0.05$) (Table 3). Cockroaches spent also significantly more time in A20379E than in MaxForce ($P < 0.05$). **Comparative analysis of cumulative time showed that cockroaches spent more time in Zyrox than in MaxForce or Vendetta** ($P < 0.05$) (Table 3).

Table 3. Matrix with statistical comparison (not different or DIFFERENT) of time cockroaches spent in each bait.

	A20379A	**A20379E**	**A15276C**	**Zyrox**	**MaxForce**	**Vendetta**
A20379A						
A20379E	Not different					
A15276C	Not different	Not different				
Zyrox	Not different	Not different	Not different			
MaxForce	DIFFERENT	DIFFERENT	Not different	DIFFERENT		
Vendetta	DIFFERENT	Not different	Not different	DIFFERENT	Not different	

(4) **Conclusion: Supplemental.** The behavioral parameters (latency, number of visits, and time spent) in each test materials were used to evaluate comparatively the way German cockroach sense or perceive these materials. In assays with the baits A20379A and Zyrox, cockroaches had positive responses in all three behavioral parameters evaluated. This meant that cockroaches reached these baits faster (latency) than cockroach food, visited them more times, and spent more time touching/consuming them. The data indicates that A20379A and Zyrox were the most palatable, and attractive test materials to German cockroach.

IV. EXECUTIVE DATA SUMMARY:

Zyrox at an application rate of 3.2oz/ l000 feet square killed German cockroaches (*Blattella germanica*) with 95.7 to 100% mortality at 10-14 days post-treatment application. Application of Zyrox (0.5%; at 3.2oz/1000 ft^2) with two reapplications resulted in 95.7% mortality of Oriental cockroach (*Blatta orientalis*) at 7 days post-treatment. Cyantraniliprole (0.5%; 3.2oz/1000ft^2) treatments with 9 reapplications resulted in 97.1% mortality of adult American cockroaches (*Periplaneta americana*) at 28 days post-treatment application.

The bait should not have been replaced twice for Oriental cockroach, and 9 times for American cockroach after the initial treatment; see the OCSPP 810.3500 Premises Treatment guideline. The label language "Reapply bait every 7 days until insect pest population is at acceptable levels" should be changed to

"Reapply as needed".

In assays with the baits A20379A and Zyrox, cockroaches had positive responses in all three behavioral parameters (latency, number of visits and time spent in each test materials) evaluated. This meant that German cockroach (*Blattella germanica*) reached these baits faster (latency) than cockroach food, visited them more times, and spent more time touching or consuming them. The data indicates that the baits A20379A, A20379E, A15276C, and Zyrox elicited orientation and arrestant behavior from German cockroach, and that A20379A (Advion cockroach gel bait) and Zyrox baits outperformed behaviorally MaxForce and Vendetta.

V. LABEL RECOMMENDATIONS: Note that no new data were submitted for flies and therefore all labeling comments are related to cockroaches only.

(1) List changes to the directions for use.
On page 9 for target pests, reference to Bait Stations as application method for cockroaches (Oriental, German, and American) should be deleted or revised as the product was not tested in bait stations. Throughout the label, language in the DFU related to "control" of cockroaches should be changed to "kill."

(2) The following marketing claims are acceptable:
Kills Oriental, German, and American cockroaches.
Kills cockroaches.
Attractive bait to German cockroaches.

(3) The following marketing claims are unacceptable:
Claims related to "control" of cockroaches

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product: N/A

(5) Make other comments/recommendations as appropriate (e.g., Note to PM).
Per MRID 51052801 the studies submitted for German, Oriental, and American cockroaches did not do a comparative evaluation resulting in 45 to 60% reduction of Zyrox versus competing brands and comparative efficacy claims with percentages are typically unacceptable. Therefore, the claim "Uses 45% to 60% less bait per square foot than competing brands" on the label with respect to cockroaches is unsubstantiated. Whilst the claim "apply at 0.2 to 0.4 pounds per 1000 square feet" is accurate, the lowest rate for cockroaches is 0.32 lbs per 1000 square feet. Finally, the product took 28 days to reach acceptable efficacy for American cockroaches so a labeling statement indicating that the product is slow acting for this species may be warranted.